PLOS ONE

REGISTERED REPORT PROTOCOL

Understanding target-specific effects of antidepressant drug pollution on molluscs: A systematic review protocol

Maurice E. Imiuwa[1,2]*, **Alice Baynes**[2], **Edwin J. Routledge**[2]*

1 Faculty of life Sciences, Department of Animal and Environmental Biology, University of Benin, Benin City, Nigeria, **2** College of Health, Medicine and Life Sciences, Brunel University London, Uxbridge, United Kingdom

* eghosamaurice.imiuwa@brunel.ac.uk (MEI); edwin.routledge@brunel.ac.uk (EJR)

This is a Registered Report and may have an associated publication; please check the article page on the journal site for any related articles.

Citation: Imiuwa ME, Baynes A, Routledge EJ (2023) Understanding target-specific effects of antidepressant drug pollution on molluscs: A systematic review protocol. PLoS ONE 18(6): e0287582. https://doi.org/10.1371/journal.pone.0287582

Editor: Peter P. Fong, Gettysburg College, UNITED STATES

Received: March 26, 2023

Accepted: June 6, 2023

Published: June 27, 2023

Peer Review History: PLOS recognizes the benefits of transparency in the peer review process; therefore, we enable the publication of all of the content of peer review and author responses alongside final, published articles. The editorial history of this article is available here: https://doi.org/10.1371/journal.pone.0287582

Abstract

Background

The environmental prevalence of widely prescribed human pharmaceuticals that target key evolutionary conserved biomolecules present across phyla is concerning. Antidepressants, one of the most widely consumed pharmaceuticals globally, have been developed to target biomolecules modulating monoaminergic neurotransmission, thus interfering with the endogenous regulation of multiple key neurophysiological processes. Furthermore, rising prescription and consumption rates of antidepressants caused by the burgeoning incidence of depression is consistent with increasing reports of antidepressant detection in aquatic environments worldwide. Consequently, there are growing concerns that long-term exposure to environmental levels of antidepressants may cause adverse drug target-specific effects on non-target aquatic organisms. While these concerns have resulted in a considerable body of research addressing a range of toxicological endpoints, drug target-specific effects of environmental levels of different classes of antidepressants in non-target aquatic organisms remain to be understood. Interestingly, evidence suggests that molluscs may be more vulnerable to the effects of antidepressants than any other animal phylum, making them invaluable in understanding the effects of antidepressants on wildlife. Here, a protocol for the systematic review of literature to understand drug target-specific effects of environmental levels of different classes of antidepressants on aquatic molluscs is described. The study will provide critical insight needed to understand and characterize effects of antidepressants relevant to regulatory risk assessment decision-making, and/or direct future research efforts.

Methods

The systematic review will be conducted in line with the guidelines by the Collaboration for Environmental Evidence (CEE). A literature search on Scopus, Web of Science, PubMed, as well as grey literature databases, will be carried out. Using predefined criteria, study selection, critical appraisal and data extraction will be done by multiple reviewers with a web-based evidence synthesis platform. A narrative synthesis of outcomes of selected

Data Availability Statement: All relevant data from this study will be made available upon study completion.

Funding: MEI received funding from Tertiary Education Trust Fund (TETFund), Nigeria (https://tetfund.gov.ng/). The funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing interests: The authors have declared that no competing interests exist.

studies will be presented. The protocol has been registered in the Open Science Framework (OSF) registry with the registration DOI: 10.17605/OSF.IO/P4H8W.

Introduction

The widespread occurrence of human pharmaceuticals in the environment is a cause of increasing concern. Particularly worrisome is the presence, in the aquatic environment, of neuromodulatory pharmaceuticals developed to specifically target critical-function biomolecules such as monoamine neurotransmitter re-uptake transporters, their synaptic receptors and deamination enzymes in humans, that are well conserved across animal phyla [1–5]. Monoamine neurotransmitters are biogenic amines containing one amine group (and essentially include serotonin, norepinephrine and dopamine), that are critical in the modulation of virtually all brain functions, and play key roles in the regulation of physiological processes such as development, reproduction, autonomic functions, hormone secretion and complex behaviours [6–9]. The synaptic activity of monoamines is tightly modulated by their re-uptake transporters, pre-and post-synaptic receptors and deaminating oxidases [6,10,11]. These critical-function biomolecules regulate the intensity and duration of synaptic monoamine signaling, and for this reason, they are key pharmacological targets for antidepressant drugs [6,12]. Antidepressants are a major class of psychotropic drugs that target and inhibit monoamine re-uptake transporters, their synaptic receptors and terminating enzymes, thereby interfering with the endogenous modulation of monoaminergic neurotransmission, a key neurophysiological process [13]. They are used for the treatment of depression, and are also prescribed for other disorders such as generalized anxiety disorders, obsessive-compulsive disorder, panic disorder, social anxiety disorder and specific phobia [14–16].

Based on their modes of action and chemical structures, antidepressants are classified into four major groups: monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), and serotonin-norepinephrine reuptake inhibitors (SNRIs) [17,18]. Additionally, however, a fifth group of largely heterogenous antidepressant drugs exists, and are accordingly, referred to as 'atypical' or 'other' antidepressants [19]. Briefly, MAOIs exert inhibitory action on monoamine oxidases (the enzymes that oxidatively deaminate monoamine neurotransmitters). TCAs, named after their tricyclic chemical structures, inhibit serotonin and norepinephrine re-uptake transporters, and also exert antagonistic actions on post-synaptic adrenergic α_1 and α_2, muscarinic and histamine H_1 receptors. SNRIs like TCAs also inhibit serotonin and norepinephrine re-uptake transporters, but they do so with little, or no, pharmacological action on the post-synaptic receptors affected by TCAs. SSRIs act therapeutically as selective inhibitors of serotonin reuptake transporters, while atypical antidepressants exert a range of pharmacological actions on monoamine neurotransmitter system including acting as antagonists and agonists of several pre- and post-synaptic receptors, and inhibitors of serotonin, norepinephrine and dopamine transmembrane transporters [13,19].

Interestingly, in recent times the prescription and consumption of antidepressants have consistently been on the increase due to a burgeoning prevalence of depression in society [20,21]. Indeed, depression is projected to become the leading cause of disease morbidity worldwide by 2030 [20,22,23]. Although readily biotransformed following consumption by patients, antidepressant drugs are essentially excreted as parent compounds and pharmaceutically active metabolites [24–29]. As they are not completely removed by wastewater treatment processes [30,31], antidepressant drugs end up in wastewater effluents discharged into surface

waters [32–34], and in sewage sludge or reclaimed water applied to agricultural land [35]. The fallout of this has been their widespread occurrence and detection in the aquatic environments across the globe, with different antidepressant drugs and their active metabolites detected in soil, ground water, surface water and wildlife [34,36–39]. While current environmental antidepressant levels range from ng/L to low μg/L, they are designed to act on their molecular targets at particularly low concentrations [40,41]. Consequently, investigations into potential effects of exposure to antidepressants in wildlife have been on the increase owing to their known neuromodulatory effects in humans [42,43]. There are now a considerable number of laboratory studies describing a range of toxicological effects following exposure to various antidepressants in different aquatic species. However, drug target-specific effects of different classes of antidepressants in non-target aquatic organisms remain to be understood [18,41,43,44]. Importantly, data suggest molluscs may be more vulnerable to the effects of antidepressants than any other animal phylum because multiple key physiological processes (including reproduction and development) are regulated by monoamines rather than vertebrate-type sex steroids in molluscs. To illustrate, in vertebrates the enzyme 5α-reductase is involved in the conversion of testosterone to the more potent form, dihydrotestosterone (DHT), which is important for the formation of male phenotype and the development of external genitalia during embryogenesis [45–47]. However, inhibition of 5α-reductase during early development in the freshwater pulmonate gastropods, *Biomphalaria glabrata* and *Physella acuta*, has been shown to affect shell formation [48], and to date, no androgen receptor (the target for DHT action) has been identified in molluscs [49–52], while monoamines have been reported to have a role in shell formation in the Pacific oyster, *Crassostrea gigas*. [53,54]. Furthermore, in the bivalves, *Nodipecten subnosus*, *Crassostrea gigas* and *Argopecten purpuratus*, monoamines are detected in the gonads, with increased concentrations during gonadal growth stages, which decrease after spawning [55–57], suggesting a direct role in reproduction. Additionally, in freshwater pulmonate gastropods including *Biomphalaria glabrata*, dopamine is detected in the albumen gland with increased concentrations during perivitelline fluid secretion, while in *Helisoma duryi*, it is involved in perivitelline fluid secretion [58,59]. In *Helisoma trivolvis*, serotonin is involved in larval development via serotonin receptor-modulated cAMP-dependent regulation of cell division [8].

Molluscs are a highly biodiverse group (second only to arthropods in terms of number of species), displaying a wide variety of ecologically unique body forms, sizes, lifestyles, and microhabitat preferences [60,61]. This makes them indispensable for understanding ecological effects of anthropogenic chemicals in the aquatic environments. Molluscan monoamines are produced by the nervous system where they mediate chemical communication between neurons, with other innervated cell types, or exert hormonal action when released into the blood [62–65]. There are also hormone-producing neurons, the neurosecretory cells, which together with their targets, form the neuroendocrine system that is the main source of hormones in molluscs [61,66]. Interestingly, targets for antidepressant action, including monoamine transmembrane transporters, monoamine synaptic receptors and monoamine oxidases, are present in molluscs [67–72], and the effective concentrations of antidepressant drugs in molluscs are in the range of those commonly detected in the aquatic environment [73–75]. Also, the need to consider the effects of substances of high environmental relevance and poor scientific underpinning in molluscs has long been recognized as a priority area [76].

While there are reviews on general effects of antidepressants on aquatic organisms (with data on molluscs), including Fong and Ford [77], published almost 10 years ago; Silva et al. [78], with scope limited to SSRIs; Sehonova et al. [42] and Moreira et al. [79], with very brief sections on molluscan data; and Canesi et al. [80], limited to bivalves, they are all narrative reviews. Based on continued research interest, a considerable number of individual studies on

different pertinent aspects of the subject now exist. The present study, therefore, seeks to understand target-specific effects of environmental levels of different classes of antidepressants in molluscs through a systematic review of literature. The study provides the opportunity to (i) synthesize the first systematic review of the effects of exposure of aquatic molluscs to different classes of antidepressant drugs, with the potential to provide critical insight relevant to regulatory risk assessment decision-making, (ii) identify research gaps in our current understanding of their mechanisms of action, (iii) establish best practice within research studies to improve future work in the field, and (iv) identify questions for which available evidence provide clear answers and further research may not be necessary. The authors are solely responsible for the design and conduct of the study, and it does not involve any form of external organizational stakeholder engagement.

Objective of the review

Primary question. The primary question of the study is: what are the target-specific effects of environmental levels of different classes of antidepressant drugs on aquatic molluscs? The primary question consists of the following PECO (population, exposure, comparator and outcome) components—Population: molluscs (all aquatic species and all life stages) exposed to laboratory-based water-borne antidepressants; Exposure: acute/chronic exposure to any class of antidepressants and/or their major pharmaceutically active metabolites; Comparator: vehicle-treated or naïve controls; Outcome: all study outcomes directly related to behaviour, movement, feeding, respiration, reproduction, development, immunity, neurophysiology, and intercellular signaling events.

Methods

The systematic review will be conducted in line with the guidelines by the Collaboration for Environmental Evidence (CEE) [81]. Accordingly, the systematic review protocol was developed following the CEE Reporting standards for Systematic Evidence Synthesis (ROSES) [82] (See S1 Table for ROSES; S2 Table for PRISMA-P in compliance with PLOS One protocol publication criteria). As recommended by Whaley et al. [83], the protocol has been registered in the Open Science Framework (OSF) registry, with the Registration DOI: 10.17605/OSF.IO/P4H8W.

Searching for articles

While two bibliographic databases are usually considered sufficient for evidence synthesis involving animal studies [84], prioritizing sources with the largest number of relevant articles has been suggested [85]. Consequently, article searches will be conducted in three key bibliographic databases, namely Web of science, Scopus and PubMed. The search strategy outlined in Table 1, comprehensively includes key study population and exposure terms for peer-reviewed original research articles in English language using information retrieval sensitivity and relevance criteria for each of the databases. The search strategy was developed in consultation with an academic liaison librarian as recommended for evidence synthesis [86]. Further, as supplementary searches for grey literature in catalogues of academic theses, databases of conferences and proceedings, preprint servers and funders' databases of on-going research have been recommended for mitigating publication bias in systematic reviews [87], additional searches will be conducted in ProQuest Dissertations and Theses Global, Open Access Theses and Dissertations, OpenGrey, Grey Literature Report, Research square and EcoEvoRxiv for grey literature. The supplementary searches will be carried out using key study terms [88].

Table 1. Study search strategy for use in Scopus, Web of Science and PubMed.

Bibliographic databases	Search strings
Scopus	(TITLE-ABS-KEY (mollusc* OR gastropod* OR mussel* OR clam OR clams OR bivalves OR mollusk* OR snail* OR cuttlefish) AND TITLE-ABS-KEY ("psychotropic drug*" OR antidepressants OR sertraline OR fluoxetine OR citalopram OR paroxetine OR amitriptyline OR venlafaxine OR mirtazapine OR dosulepin OR clomipramine OR dosulepin OR escitalopram OR fluvoxamine OR imipramine OR nortriptyline OR lofepramine)) AND (LIMIT-TO (DOCTYPE, "ar"))
Web of Science, PubMed	(Mollusc* OR Gastropod* OR Mussel* OR Clam OR clams OR Bivalves OR Mollusk* OR Snail* OR cuttlefish) AND ("psychotropic drug*" OR Antidepressants OR Sertraline OR Fluoxetine OR Citalopram OR paroxetine OR amitriptyline OR venlafaxine OR mirtazapine OR Dosulepin OR Clomipramine OR Dosulepin OR Escitalopram OR Fluvoxamine OR Imipramine OR Nortriptyline OR Lofepramine)

https://doi.org/10.1371/journal.pone.0287582.t001

Article screening and study eligibility criteria

Screening process. A web-based evidence synthesis platform, EPPI-Reviewer [89], will be used to manage article search across all selected databases. In the first phase, articles will be screened using only titles and abstracts within EPPI-Reviewer to facilitate uniform review by two reviewers. The outcome of this screening phase will then be evaluated by both reviewers for correctness, and a third reviewer will be contacted to provide an independent opinion in the event of any discrepancy. In the second phase, the full text of articles that have been selected and approved in the first phase are then screened against the pre-defined inclusion and exclusion criteria shown in Table 2 by two reviewers. In the final phase, full text-screened articles that are selected and approved by the two reviewers using the study PECO-based inclusion and exclusion criteria will be included in the study. This procedure will be replicated for grey literature.

Table 2. Study inclusion and exclusion criteria.

Study parameters	Inclusion criteria	Exclusion criteria
Study design	Waterborne antidepressant laboratory exposures	*In vitro* studies, feed-borne exposure, injection of antidepressants
Population	All genera/species and life stages of aquatic molluscs	Molluscan cell lines, land molluscs, any other animal phylum
Exposure	Exposure to all classes of antidepressants (parent compound/active metabolites) singly administered	Antidepressant mixtures, other pharmaceuticals/xenobiotics
Outcome measures	Effects on behaviour, locomotion, respiration, feeding, reproduction, development, immunity, neurophysiology, and intracellular signalling events	Any general toxicity effects including biotransformation, cytotoxicity, cytogenetics and mortality
Language	English	Any other language
Publication date	No restriction	No restriction
Others	Nil	Nil

https://doi.org/10.1371/journal.pone.0287582.t002

Eligibility criteria. As the study seeks to understand the effects of antidepressants in the aquatic environment on aquatic molluscs, only whole-animal laboratory studies, and not *in vitro* exposure studies, will be included. Additionally, since the pharmaceuticals of interest are antidepressants that are widely detected in the aquatic environment, only waterborne antidepressant exposure studies will be included. As a result, studies on other routes of exposure, including foodborne antidepressants and injection of antidepressants will not be included. On account of the habitat of interest, only aquatic molluscs (all life stages), and not terrestrial species, will be eligible for inclusion. With regard to test chemical eligibility criteria, laboratory exposure studies on all antidepressant drugs and their major active metabolites (since pharmacologically active metabolites of antidepressants are also widely detected in the aquatic environment) will be included. Furthermore, since it is difficult to delineate constituent chemical effects in mixture exposures [90], only studies using singly administered antidepressants will be included. However, studies containing data on both mixtures and singly administered antidepressants will be included in order to extract data for singly administered antidepressants only.

Antidepressants are designed to pharmacologically target monoamine re-uptake transporters, pre-and post-synaptic receptors of monoaminergic neurons, and monoamine oxidases. In molluscs, monoamines have been shown to have functions in key physiological processes including behaviour [91,92], locomotion [93,94], respiration [95,96], feeding [97,98], reproduction [57,59] development [8,99] and immunity [100]. As a result, outcome data directly related to these physiological processes will be included in the study. Furthermore, as recent studies have revealed that in addition to monoaminergic system, other neural targets especially those directly involved in the regulation of neuronal survival, neuronal growth and synaptic plasticity, may play more direct roles in antidepressant effects [101,102], outcome data on neurophysiology, and intracellular signaling events will be included in the study. Conversely, study outcomes other than those selected by these criteria including biotransformation, cytotoxicity, cytogenetics, mortality and any other general toxicity effects will not be included in the review. On the whole, external validity, the relevance of each included study to the systematic review question [103,104], was centrally factored into the eligibility criteria development.

Study validity assessment. 'Internal validity', 'risk of bias' or 'critical appraisal' generally describes the quality assessment of each of the included studies in a systematic review [103]. The assessment is usually based on a set of questions defined in advance to address various types of bias [105]. In environmental science, this is generally flexible, and the development and operationalization of specific internal validity assessment tools depend on a number of key study design and performance parameters [104]. Consequently, a comprehensive set of quality parameters bordering on study design and performance were defined for the risk of bias assessment of each included study in this systematic review (Table 3) while adopting a framework of select sources of bias [86,105]. Specifically, our tool is framed into a set of 10 questions which requires a yes-or-no answer. The answers (yes = 1; no = 0) to the quality questions for each of the included studies are summed to further classify each study into any of three quality categories, namely low risk of bias ($\geq$ 8), medium risk of bias (6–7) and high risk of bias ($\leq$ 5). The appraisal will be done by one reviewer, and evaluated by three reviewers for completeness and consistency.

Data extraction. All data on the systematic review PECO statement including study ID (or authors and the year of publication) and data on all study characteristics of each included study will be extracted. Data extraction will be carried out on EPPI-Reviewer platform to facilitate uniform extraction. Extraction will be carried out by one reviewer, while extracted data will be evaluated by two independent reviewers for completeness and consistency. Where there are incomplete data, authors will be contacted for clarifications. Finally, extracted data will be made available as an additional data file.

Table 3. Study critical appraisal framework.

Key study parameter questions	Study ID		Study ID		Study ID	
	Yes	No	Yes	No	Yes	No
Were the control and treatment groups similar at baseline?						
Is there any difference in the way the control and treatment groups were handled during the experiment (apart from difference due to treatment)?						
Was the experiment replicated?						
Was an appropriate control provided?						
Were the exposure concentrations experimentally determined in the exposure medium?						
Is it likely that the water renewal level and frequency are sufficient to maintain exposure conditions?						
Are the test concentrations environmentally relevant or were the internal (tissue) levels determined?						
Is there any difference in the way the outcome measures in both control and treatment groups were accessed?						
Is there selective reporting in the way the outcome measures are presented and reported?						
Is the study free from any other form of bias of concern not listed here?						
Summation	≥ 8		6–7		≤ 5	
Risk of bias level	low risk of bias		medium risk of bias		high risk of bias	

https://doi.org/10.1371/journal.pone.0287582.t003

Potential effect modifiers. Potential effect modifiers, or factors that may cause some degree of heterogeneity in the response of molluscs exposed to antidepressants, will be extracted from each included study and considered in the review. We have selected the following key potential effect modifiers associated with toxicological responses of biological systems to chemical exposure:

- Species, sex, reproductive strategy, life stage and chosen endpoints
- Antidepressant class and exposure concentrations
- Exposure duration, renewal regime and percentage renewal

Data synthesis, presentation and discussion

Given the wide variety of aquatic molluscan species, classes of antidepressant drugs and exposure conditions reported in laboratory studies, the data are not considered to be amenable to meta-analysis [105], and only narrative synthesis will be conducted. Accordingly, data on all study characteristics and statistically significant results of each included study will be presented with tables [105]. Further, data within distinct subgroups comprising species of molluscs, class of antidepressants, exposure concentrations and nature of effects will be summarized, compared and contrasted [106]. The synthesis will be followed by an extensive discussion. Where

full text-screened articles are excluded from data synthesis, a list of affected studies with the reason for exclusion will be provided. The EPPI-Centre approach to assessing the overall robustness of the synthesis will be adopted, and described in terms of the internal validity of included studies [107].

Supporting information

S1 Table. ROSES.
(XLSX)

S2 Table. PRISMA-P.
(DOCX)

Acknowledgments

The authors would like to thank Joanne Mcphie, an academic liaison librarian, Brunel University London, for technical assistance with the search strategy development.

Author Contributions

Conceptualization: Maurice E. Imiuwa, Alice Baynes, Edwin J. Routledge.

Methodology: Maurice E. Imiuwa.

Writing – original draft: Maurice E. Imiuwa.

Writing – review & editing: Alice Baynes, Edwin J. Routledge.

References

1. D'Aniello E, Paganos P, Anishchenko E, D'Aniello S, Arnone MI. Comparative Neurobiology of Biogenic Amines in Animal Models in Deuterostomes. Front Ecol Evol. 2020; 8(September):1–13.
2. Burman C, Maqueira B, Coadwell J, Evans PD. Eleven new putative aminergic G-protein coupled receptors from Amphioxus (Branchiostoma floridae): Identification, sequence analysis and phylogenetic relationship. Invertebr Neurosci. 2007; 7(2):87–98. https://doi.org/10.1007/s10158-006-0041-z PMID: 17225134
3. Tierney AJ. Invertebrate serotonin receptors: A molecular perspective on classification and pharmacology. J Exp Biol. 2018; 221(19). https://doi.org/10.1242/jeb.184838 PMID: 30287590
4. Gunnarsson L, Jauhiainen A, Kristiansson E, Nerman O, Larsson DGJ. Evolutionary conservation of human drug targets in organisms used for environmental risk assessments. Environ Sci Technol. 2008; 42(15):5807–13. https://doi.org/10.1021/es8005173 PMID: 18754513
5. McRobb FM, Sahagún V, Kufareva I, Abagyan R. In silico analysis of the conservation of human toxicity and endocrine disruption targets in aquatic species. Environ Sci Technol. 2014; 48(3):1964–72. https://doi.org/10.1021/es404568a PMID: 24392850
6. Torres GE, Gainetdinov RR, Caron MG. Plasma membrane monoamine transporters: Structure, regulation and function. Nat Rev Neurosci. 2003; 4(1):13–25. https://doi.org/10.1038/nrn1008 PMID: 12511858
7. Berger M, Gray JA, Roth BL. The expanded biology of serotonin. Annu Rev Med. 2009; 60(February):355–66. https://doi.org/10.1146/annurev.med.60.042307.110802 PMID: 19630576
8. Glebov K, Voronezhskaya EE, Khabarova MY, Ivashkin E, Nezlin LP. Mechanisms underlying dual effects of serotonin during development of Helisoma trivolvis (Mollusca). 2014; 14:1–19. https://doi.org/10.1186/1471-213X-14-14 PMID: 24625099
9. Sasaki M, Shibata E, Tohyama K, Kudo K, Endoh J, Otsuka K, et al. Monoamine neurons in the human brain stem: Anatomy, magnetic resonance imaging findings, and clinical implications. Neuroreport. 2008; 19(17):1649–54. https://doi.org/10.1097/WNR.0b013e328315a637 PMID: 18852680
10. Costa L, Trovato C, Musumeci SA, Catania M V., Ciranna L. 5-HT1A and 5-HT7 receptors differently modulate AMPA receptor-mediated hippocampal synaptic transmission. Hippocampus. 2012; 22(4):790–801. https://doi.org/10.1002/hipo.20940 PMID: 21538661

11. Bortolato M, Chen K, Shih JC. Monoamine oxidase inactivation: From pathophysiology to therapeutics. Adv Drug Deliv Rev. 2008; 60(13–14):1527–33. https://doi.org/10.1016/j.addr.2008.06.002 PMID: 18652859

12. Barra Caracciolo A, Topp E, Grenni P. Pharmaceuticals in the environment: Biodegradation and effects on natural microbial communities. A review. J Pharm Biomed Anal [Internet]. 2015; 106:25–36. Available from: http://dx.doi.org/10.1016/j.jpba.2014.11.040s PMID: 25534003

13. Hillhouse TM, Porter JH. A brief history of the development of antidepressant drugs: From monoamines to glutamate. Exp Clin Psychopharmacol. 2015; 23(1):1–21. https://doi.org/10.1037/a0038550 PMID: 25643025

14. Marken PA, Munro SJ. Selecting a Selective Serotonin Reuptake Inhibitor: Clinically Important Distinguishing Features. Prim Care Companion J Clin Psychiatry. 2000; 2(6):205–10. https://doi.org/10.4088/pcc.v02n0602 PMID: 15014630

15. Sinclair L, Nutt D. Anxiolytics. Psychiatry. 2007; 6(7):284–8.

16. Racagni G, Popoli M. The pharmacological properties of antidepressants. Int Clin Psychopharmacol. 2010; 25(3):117–31. https://doi.org/10.1097/YIC.0b013e3283311acd PMID: 20305568

17. Tang SW, Helmeste DM, Leonard BE. Antidepressant compounds: A critical review. In: Depression: From Psychopathology to Pharmacotherapy. 2010. p. 1–19.

18. Castillo-Zacarías C, Barocio ME, Hidalgo-Vázquez E, Sosa-Hernández JE, Parra-Arroyo L, López-Pacheco IY, et al. Antidepressant drugs as emerging contaminants: Occurrence in urban and non-urban waters and analytical methods for their detection. Sci Total Environ. 2021; 757. https://doi.org/10.1016/j.scitotenv.2020.143722 PMID: 33221013

19. Schwasinger-Schmidt TE, Macaluso M. Other Antidepressants. In: Handbook of Experimental Pharmacology. 2018. p. 325–55.

20. Luo Y, Kataoka Y, Ostinelli EG, Cipriani A, Furukawa TA. National Prescription Patterns of Antidepressants in the Treatment of Adults With Major Depression in the US Between 1996 and 2015: A Population Representative Survey Based Analysis. Front Psychiatry. 2020; 11(35):1–11.

21. Soleymani F, Taheri F, Roughead E, Nikfar S, Abdollahi M. Pattern of antidepressant utilization and cost in Iran from 2006 to 2013 in comparison with other countries. J Epidemiol Glob Health. 2018; 8(3–4):213–9. https://doi.org/10.2991/j.jegh.2018.06.101 PMID: 30864766

22. Kang J, Wang D, Duan Y, Zhai L, Shi L, Guo F. Aerobic exercise prevents depression via alleviating hippocampus injury in chronic stressed depression rats. Brain Sci. 2021; 11(1):1–12.

23. WHO. Global burden of mental disorders and the need for a comprehensive, coordinated response from health and social sectors at the country level. World Health Organization. 2011.

24. Li H, Sumarah MW, Topp E. Persistence of the tricyclic antidepressant drugs amitriptyline and nortriptyline in agriculture soils. Environ Toxicol Chem. 2013; 32(3):509–16. https://doi.org/10.1002/etc.2112 PMID: 23280809

25. Stimmel GL, Dopheide JA, Stahl SM. Mirtazapine: An Antidepressant with Noradrenergic and Specific Serotonergic Effects. Pharmacother J Hum Pharmacol Drug Ther. 1997; 17(1):10–21. PMID: 9017762

26. Magalhães P, Alves G, Llerena A, Falcão A. Venlafaxine pharmacokinetics focused on drug metabolism and potential biomarkers. Drug Metabol Drug Interact. 2014; 29(3):129–41. https://doi.org/10.1515/dmdi-2013-0053 PMID: 24607919

27. Devane CL, Liston HL, Markowitz JS. Clinical Pharmacokinetics of Sertraline. Clin Pharmacokinet. 2002; 41(15):1247–66. https://doi.org/10.2165/00003088-200241150-00002 PMID: 12452737

28. Wenthur CJ, Bennett MR, Lindsley CW. Classics in chemical neuroscience: Fluoxetine (Prozac). ACS Chem Neurosci. 2014; 5(1):14–23.

29. Sangkuhl K, Klein TE, Altman RB. PharmGKB summary: Citalopram pharmacokinetics pathway. Pharmacogenet Genomics. 2011; 21(11):769–72. https://doi.org/10.1097/FPC.0b013e328346063f PMID: 21546862

30. Lajeunesse A, Smyth SA, Barclay K, Sauvé S, Gagnon C. Distribution of antidepressant residues in wastewater and biosolids following different treatment processes by municipal wastewater treatment plants in Canada. Water Res. 2012; 46(17):5600–12. https://doi.org/10.1016/j.watres.2012.07.042 PMID: 22898669

31. Metcalfe CD, Chu S, Judt C, Li H, Oakes KD, Servos MR, et al. Antidepressants and their metabolites in municipal wastewater, and downstream exposure in an urban watershed. Environ Toxicol Chem. 2010; 29(1):79–89. https://doi.org/10.1002/etc.27 PMID: 20821422

32. Giebułtowicz J, Nałecz-Jawecki G. Occurrence of antidepressant residues in the sewage-impacted Vistula and Utrata rivers and in tap water in Warsaw (Poland). Ecotoxicol Environ Saf. 2014; 104(1):103–9. https://doi.org/10.1016/j.ecoenv.2014.02.020 PMID: 24636953

33. Schultz MM, Furlong ET. Trace analysis of antidepressant pharmaceuticals and their select degradates in aquatic matrixes by LC/ESI/MS/MS. Anal Chem. 2008; 80(5):1756–62. https://doi.org/10.1021/ac702154e PMID: 18229944

34. dan Ma L, Li J, Li J jun, Liu M, zhi Yan D, yan Shi W, et al. Occurrence and source analysis of selected antidepressants and their metabolites in municipal wastewater and receiving surface water. Environ Sci Process Impacts. 2018; 20(7):1020–9. https://doi.org/10.1039/c8em00077h PMID: 29897361

35. Kinney CA, Furlong ET, Werner SL, Cahill JD. Presence and distribution of wastewater-derived pharmaceuticals in soil irrigated with reclaimed water. Environ Toxicol Chem. 2006; 25(2):317–26. https://doi.org/10.1897/05-187r.1 PMID: 16519291

36. Grabicova K, Grabic R, Fedorova G, Fick J, Cerveny D, Kolarova J, et al. Bioaccumulation of psychoactive pharmaceuticals in fish in an effluent dominated stream. Water Res [Internet]. 2017; 124:654–62. Available from: https://doi.org/10.1016/j.watres.2017.08.018 PMID: 28825984

37. Xiang J, Wu M, Lei J, Fu C, Gu J, Xu G. The fate and risk assessment of psychiatric pharmaceuticals from psychiatric hospital effluent. Ecotoxicol Environ Saf [Internet]. 2018; 150(September 2017):289–96. Available from: https://doi.org/10.1016/j.ecoenv.2017.12.049 PMID: 29289864

38. Schultz MM, Furlong ET, Kolpin DW, Werner SL, Schoenfuss HL, Barber LB, et al. Antidepressant pharmaceuticals in two U.S. effluent-impacted streams: Occurrence and fate in water and sediment and selective uptake in fish neural tissue. Environ Sci Technol. 2010; 44(6):1918–25. https://doi.org/10.1021/es9022706 PMID: 20121081

39. Richmond EK, Rosi EJ, Walters DM, Fick J, Hamilton SK, Brodin T, et al. A diverse suite of pharmaceuticals contaminates stream and riparian food webs. Nat Commun [Internet]. 2018; 9(1):1–9. Available from: http://dx.doi.org/10.1038/s41467-018-06822-w.

40. Regenthal R, Krueger M, Koeppel C, Preiss R. Drug levels: Therapeutic and toxic serum/plasma concentrations of common drugs. J Clin Monit Comput. 1999; 15(7–8):529–44. https://doi.org/10.1023/a:1009935116877 PMID: 12578052

41. Franzellitti S, Buratti S, Valbonesi P, Fabbri E. The mode of action (MOA) approach reveals interactive effects of environmental pharmaceuticals on Mytilus galloprovincialis. Aquat Toxicol [Internet]. 2013;140–141:249–56. Available from: http://dx.doi.org/10.1016/j.aquatox.2013.06.005.

42. Sehonova P, Svobodova Z, Dolezelova P, Vosmerova P, Faggio C. Effects of waterborne antidepressants on non-target animals living in the aquatic environment: A review. Sci Total Environ [Internet]. 2018;631–632:789–94. Available from: https://doi.org/10.1016/j.scitotenv.2018.03.076 PMID: 29727988

43. Shaliutina-Kolešová A, Shaliutina O, Nian R. The effects of environmental antidepressants on macroinvertebrates: a mini review. Water Environ J. 2020; 34(1):153–9.

44. Gould SL, Winter MJ, Norton WHJ, Tyler CR. The potential for adverse effects in fish exposed to antidepressants in the aquatic environment. Environ Sci Technol. 2021; 55(24):16299–312. https://doi.org/10.1021/acs.est.1c04724 PMID: 34856105

45. Li L, Zirkin BR, Papadopoulos V. Leydig Cell Androgen Synthesis. In: Encyclopedia of Reproduction [Internet]. Elsevier; 2018. p. 215–21. Available from: https://linkinghub.elsevier.com/retrieve/pii/B978012801238364583X.

46. Andersson S, Berman DM, Jenkins EP, Russell DW. Deletion of steroid 5α-reductase 2 gene in male pseudohermaphroditism. Nature. 1991; 354(6349):159–61.

47. García-García M, Sánchez-Hernández M, García-Hernández MP, García-Ayala A, Chaves-Pozo E. Role of 5α-dihydrotestosterone in testicular development of gilthead seabream following finasteride administration. J Steroid Biochem Mol Biol [Internet]. 2017; 174(April):48–55. Available from: http://dx.doi.org/10.1016/j.jsbmb.2017.07.024.

48. Baynes A, Montagut Pino G, Duong GH, Lockyer AE, McDougall C, Jobling S, et al. Early embryonic exposure of freshwater gastropods to pharmaceutical 5-alpha-reductase inhibitors results in a surprising open-coiled "banana-shaped" shell. Sci Rep [Internet]. 2019; 9(1):1–12. Available from: http://dx.doi.org/10.1038/s41598-019-52850-x.

49. Kaur S, Baynes A, Lockyer AE, Routledge EJ, Jones CS, Noble LR, et al. Steroid Androgen Exposure during Development Has No Effect on Reproductive Physiology of Biomphalaria glabrata. Lukowiak K, editor. PLoS One [Internet]. 2016 Jul 22; 11(7):e0159852. Available from: https://dx.plos.org/10.1371/journal.pone.0159852. https://doi.org/10.1371/journal.pone.0159852 PMID: 27448327

50. Kaur S, Jobling S, Jones CS, Noble LR, Routledge EJ, Lockyer AE. The nuclear receptors of Biomphalaria glabrata and Lottia gigantea:Implications for developing new model organisms. PLoS One. 2015; 10(4):1–23. https://doi.org/10.1371/journal.pone.0121259 PMID: 25849443

51. Vogeler S, Galloway TS, Lyons BP, Bean TP. The nuclear receptor gene family in the Pacific oyster, Crassostrea gigas, contains a novel subfamily group. BMC Genomics. 2014; 15(1):1–15. https://doi.org/10.1186/1471-2164-15-369 PMID: 24885009

52. Baker ME. Steroid receptors and vertebrate evolution. Mol Cell Endocrinol [Internet]. 2019; 496 (July):110526. Available from: https://doi.org/10.1016/j.mce.2019.110526 PMID: 31376417

53. Liu Z, Wang L, Yan Y, Zheng Y, Ge W, Li M, et al. D1 dopamine receptor is involved in shell formation in larvae of Pacific oyster Crassostrea gigas. Dev Comp Immunol [Internet]. 2018; 84:337–42. Available from: https://doi.org/10.1016/j.dci.2018.03.009 PMID: 29550270

54. Liu Z, Zhou Z, Zhang Y, Wang L, Song X, Wang W, et al. Ocean acidification inhibits initial shell formation of oyster larvae by suppressing the biosynthesis of serotonin and dopamine. Sci Total Environ [Internet]. 2020; 735:139469. Available from: https://doi.org/10.1016/j.scitotenv.2020.139469 PMID: 32498014

55. Osada M, Nomura T. Seasonal Variations of Catecholamine Levels in the TIssues of the Japanese Oyster, Crassostrea gigas. Comp Biochem Physiol. 1989; 93(1):171–3.

56. Martínez G, Rivera A. Role of monoamines in the reproductive process of argopecten purpuratus. Invertebr Reprod Dev. 1994; 25(2):167–74.

57. López-Sánchez JA, Maeda-Martínez AN, Croll RP, Acosta-Salmón H. Monoamine fluctuations during the reproductive cycle of the Pacific lion's paw scallop Nodipecten subnodosus. Comp Biochem Physiol—A Mol Integr Physiol. 2009; 154(3):425–8. https://doi.org/10.1016/j.cbpa.2009.07.021 PMID: 19651231

58. Boyle JP, Yoshino TP. Monoamines in the albumen gland, plasma, and central nervous system of the snail Biomphalaria glabrata during egg-laying. Comp Biochem Physiol—A Mol Integr Physiol. 2002; 132(2):411–22. https://doi.org/10.1016/s1095-6433(02)00091-0 PMID: 12020657

59. Mukai ST, Kiehn L, Saleuddin ASM. Dopamine stimulates snail albumen gland glycoprotein secretion through the activation of a D1-like receptor. J Exp Biol. 2004; 207(14):2507–18. https://doi.org/10.1242/jeb.01052 PMID: 15184522

60. Pandian TJ. Reproduction and Development in Mollusca [Internet]. Reproduction and Development in Mollusca. Boca Raton: CRC Press; 2018. 304 p. Available from: https://www.taylorfrancis.com/books/9781351779654.

61. Matthiessen P. An assessment of endocrine disruption in Mollusks and the potential for developing internationally standardized mollusk life cycle test guidelines. Integr Environ Assess Manag. 2008; 4 (3):274–84. https://doi.org/10.1897/IEAM_2008-003.1 PMID: 18393578

62. Werkman TR, De Vlieger TA, Stoof JC. Indications for a hormonal function of dopamine in the central nervous system of the snail Lymnaea stagnalis. Neurosci Lett. 1990; 108(1–2):167–72. https://doi.org/10.1016/0304-3940(90)90725-o PMID: 2304625

63. Chiang PK, Bourgeois JG, Bueding E. 5-Hydroxytryptamine and dopamine in Biomphalaria glabrata. J Parasitol [Internet]. 1974 Apr; 60(2):264–71. Available from: http://www.ncbi.nlm.nih.gov/pubmed/4821112. PMID: 4821112

64. Delgado N, Vallejo D, Miller MW. Localization of serotonin in the nervous system of Biomphalaria glabrata, an intermediate host for schistosomiasis. J Comp Neurol. 2012; 520(14):3236–55. https://doi.org/10.1002/cne.23095 PMID: 22434538

65. Werkman TR, van Minnen J, Voorn P, Steinbusch HWM, Westerink BHC, De Vlieger TA, et al. Localization of dopamine and its relation to the growth hormone producing cells in the central nervous system of the snail Lymnaea stagnalis. Exp Brain Res. 1991; 85(1):1–9. https://doi.org/10.1007/BF00229981 PMID: 1715823

66. Hartenstein V. The neuroendocrine system of invertebrates: A developmental and evolutionary perspective. J Endocrinol. 2006; 190(3):555–70. https://doi.org/10.1677/joe.1.06964 PMID: 17003257

67. Sloley BD. Metabolism of Monoamines in Invertebrates: The Relative Importance of Monoamine Oxidase in Different Phyla. Neurotoxicology. 2004; 25(1–2):175–83. https://doi.org/10.1016/S0161-813X(03)00096-2 PMID: 14697892

68. Blais V, Bounif N, Dubé F. Characterization of a novel octopamine receptor expressed in the surf clam Spisula solidissima. Gen Comp Endocrinol [Internet]. 2010; 167(2):215–27. Available from: https://doi.org/10.1016/j.ygcen.2010.03.008 PMID: 20302871

69. Niu D, Li Z, Du Y, He S, Dong Z, Li J. Identification of a dopamine receptor in Sinonovacula constricta and its antioxidant responses. Dev Comp Immunol [Internet]. 2020; 103(October 2019):103512. Available from: https://doi.org/10.1016/j.dci.2019.103512 PMID: 31585193

70. Sugamori KS, Sunahara RK, Guan HC, Bulloch AGM, Tensen CP, Seeman P, et al. Serotonin receptor cDNA cloned from Lymnaea stagnalis. Proc Natl Acad Sci U S A. 1993; 90(1):11–5. https://doi.org/10.1073/pnas.90.1.11 PMID: 8093556

71. Edsinger E, Dölen G. A Conserved Role for Serotonergic Neurotransmission in Mediating Social Behavior in Octopus. Curr Biol. 2018; 28(19):3136–3142.e4. https://doi.org/10.1016/j.cub.2018.07.061 PMID: 30245101

72. Caveney S, Cladman W, Verellen LA, Donly C. Ancestry of neuronal monoamine transporters in the Metazoa. J Exp Biol. 2006; 209(24):4858–68. https://doi.org/10.1242/jeb.02607 PMID: 17142674

73. Di Poi C, Darmaillacq AS, Dickel L, Boulouard M, Bellanger C. Effects of perinatal exposure to waterborne fluoxetine on memory processing in the cuttlefish Sepia officinalis. Aquat Toxicol [Internet]. 2013;132–133:84–91. Available from: http://dx.doi.org/10.1016/j.aquatox.2013.02.004.

74. Lazzara R, Blázquez M, Porte C, Barata C. Low environmental levels of fluoxetine induce spawning and changes in endogenous estradiol levels in the zebra mussel Dreissena polymorpha. Aquat Toxicol [Internet]. 2012;106–107:123–30. Available from: https://doi.org/10.1016/j.aquatox.2011.11.003 PMID: 22155424

75. Fong PP, Hoy CM. Antidepressants (venlafaxine and citalopram) cause foot detachment from the substrate in freshwater snails at environmentally relevant concentrations. Mar Freshw Behav Physiol. 2012; 45(2):145–53.

76. OECD. DETAILED REVIEW PAPER (DRP) ON MOLLUSCS LIFE-CYCLE TOXICITY TESTING. Report. 2010.

77. Fong PP, Ford AT. The biological effects of antidepressants on the molluscs and crustaceans: A review. Aquat Toxicol [Internet]. 2014; 151:4–13. Available from: https://doi.org/10.1016/j.aquatox.2013.12.003 PMID: 24374179

78. Silva LJG, Pereira AMPT, Meisel LM, Lino CM, Pena A. Reviewing the serotonin reuptake inhibitors (SSRIs) footprint in the aquatic biota: Uptake, bioaccumulation and ecotoxicology. Environ Pollut. 2015; 197:127–43. https://doi.org/10.1016/j.envpol.2014.12.002 PMID: 25528447

79. Moreira DG, Aires A, de Lourdes Pereira M, Oliveira M. Levels and effects of antidepressant drugs to aquatic organisms. Comp Biochem Physiol Part—C Toxicol Pharmacol [Internet]. 2022; 256 (March):109322. Available from: https://doi.org/10.1016/j.cbpc.2022.109322 PMID: 35272041

80. Canesi L, Miglioli A, Balbi T, Fabbri E. Physiological Roles of Serotonin in Bivalves: Possible Interference by Environmental Chemicals Resulting in Neuroendocrine Disruption. Front Endocrinol (Lausanne). 2022; 13(February):1–14. https://doi.org/10.3389/fendo.2022.792589 PMID: 35282445

81. Collaboration for Environmental Evidence (CEE). Guidelines and Standards for Evidence Synthesis in Environmental Management [Internet]. Vol. Version 5. 2022. Available from: https://environmentalevidence.org/information-for-authors/.

82. Haddaway N, Macura B, Whaley P, Pullin A. ROSES for systematic review protocols. Version 1.0 [Internet]. 2017. Available from: https://environmentalevidence.org/roses/.

83. Whaley P, Aiassa E, Beausoleil C, Beronius A, Bilotta G, Boobis A, et al. Recommendations for the conduct of systematic reviews in toxicology and environmental health research (COSTER). Environ Int [Internet]. 2020; 143(May):105926. Available from: https://doi.org/10.1016/j.envint.2020.105926 PMID: 32653802

84. de Vries RBM, Hooijmans CR, Langendam MW, van Luijk J, Leenaars M, Ritskes-Hoitinga M, et al. A protocol format for the preparation, registration and publication of systematic reviews of animal intervention studies. Evidence-based Preclin Med. 2015; 2(1):e00007.

85. Livoreil B, Glanville J, Haddaway NR, Bayliss H, Bethel A, De Lachapelle FF, et al. Systematic searching for environmental evidence using multiple tools and sources. Environ Evid. 2017; 6(1):1–14.

86. Vandenberg LN, Ågerstrand M, Beronius A, Beausoleil C, Bergman Å, Bero LA, et al. A proposed framework for the systematic review and integrated assessment (SYRINA) of endocrine disrupting chemicals. Environ Heal [Internet]. 2016 Dec 14; 15(1):74. Available from: https://doi.org/10.1186/s12940-016-0156-6 PMID: 27412149

87. Haddaway NR, Bayliss HR. Shades of grey: Two forms of grey literature important for reviews in conservation. Biol Conserv [Internet]. 2015; 191:827–9. Available from: http://dx.doi.org/10.1016/j.biocon.2015.08.018.

88. Adams J, Hillier-Brown FC, Moore HJ, Lake AA, Araujo-Soares V, White M, et al. Searching and synthesising "grey literature" and "grey information" in public health: Critical reflections on three case studies. Syst Rev [Internet]. 2016; 5(1):1–11. Available from: https://doi.org/10.1186/s13643-016-0337-y PMID: 27686611

89. Thomas J, Brunton J, Graziosi S. EPPI-Reviewer 4: software for research synthesis. EPPI-Centre Software [Internet]. London: Social Science Research Unit, UCL Institute of Education.; 2010. p. 2–5. Available from: https://eppi.ioe.ac.uk/cms/er4/Features/tabid/3396/Default.aspx.

90. Hernández AF, Gil F, Lacasaña M. Toxicological interactions of pesticide mixtures: an update. Arch Toxicol. 2017; 91(10):3211–23. https://doi.org/10.1007/s00204-017-2043-5 PMID: 28845507

91. Roshchin M, Balaban PM. Neural control of olfaction and tentacle movements by serotonin and dopamine in terrestrial snail. J Comp Physiol A Neuroethol Sensory, Neural, Behav Physiol. 2012; 198 (2):145–58. https://doi.org/10.1007/s00359-011-0695-9 PMID: 22076462

92. Weiger WA. Serotonergic modulation of behaviour: A phylogenetic overview. Biol Rev. 1997; 72 (1):61–95. https://doi.org/10.1017/s0006323196004975 PMID: 9116165

93. Newcomb JM, Katz PS. Different functions for homologous serotonergic interneurons and serotonin in species-specific rhythmic behaviours. Proc R Soc B Biol Sci. 2009; 276(1654):99–108. https://doi.org/10.1098/rspb.2008.0683 PMID: 18782747

94. Pavlova GA. Effects of serotonin, dopamine and ergometrine on locomotion in the pulmonate mollusc Helix lucorum. J Exp Biol. 2001; 204(9):1625–33. https://doi.org/10.1242/jeb.204.9.1625 PMID: 11398751

95. Lukowiak K, Martens K, Orr M, Parvez K, Rosenegger D, Sangha S. Modulation of aerial respiratory behaviour in a pond snail. Respir Physiol Neurobiol. 2006; 154(1–2):61–72. https://doi.org/10.1016/j.resp.2006.02.009 PMID: 16564752

96. Syed NI, Winlow W. Morphology and electrophysiology of neurons innervating the ciliated locomotor epithelium in Lymnaea stagnalis (L.). Comp Biochem Physiol—Part A Physiol. 1989; 93(3):633–44.

97. Elliott CJH, Susswein AJ. Comparative neuroethology of feeding control in molluscs. J Exp Biol. 2002; 205(7):877–96. https://doi.org/10.1242/jeb.205.7.877 PMID: 11916985

98. Hernádi L, Kárpáti L, Gyori J, Vehovszky Á, Hiripi L. Humoral serotonin and dopamine modulate the feeding in the snail, Helix pomatia. Acta Biol Hung. 2008; 59(SUPPL.):39–46. https://doi.org/10.1556/ABiol.59.2008.Suppl.6 PMID: 18652370

99. Filla A, Hiripi L, Elekes K. Role of aminergic (serotonin and dopamine) systems in the embryogenesis and different embryonic behaviors of the pond snail, Lymnaea stagnalis. Comp Biochem Physiol—C Toxicol Pharmacol [Internet]. 2009; 149(1):73–82. Available from: https://doi.org/10.1016/j.cbpc.2008.07.004 PMID: 18682301

100. Jia Y, Yang B, Dong W, Liu Z, Lv Z, Jia Z, et al. A serotonin receptor (Cg5-HTR-1) mediating immune response in oyster Crassostrea gigas. Dev Comp Immunol [Internet]. 2018; 82:83–93. Available from: https://doi.org/10.1016/j.dci.2017.12.029 PMID: 29305167

101. Zainullina LF, Vakhitova Y V., Lusta AY, Gudasheva TA, Seredenin SB. Dimeric mimetic of BDNF loop 4 promotes survival of serum-deprived cell through TrkB-dependent apoptosis suppression. Sci Rep. 2021; 11(1). https://doi.org/10.1038/s41598-021-87435-0 PMID: 33833366

102. Cubillos S, Engmann O, Brancato A. BDNF as a Mediator of Antidepressant Response: Recent Advances and Lifestyle Interactions. Int J Mol Sci. 2022; 23(22). https://doi.org/10.3390/ijms232214445 PMID: 36430921

103. Rooney AA, Cooper GS, Jahnke GD, Lam J, Morgan RL, Boyles AL, et al. How credible are the study results? Evaluating and applying internal validity tools to literature-based assessments of environmental health hazards. Environ Int [Internet]. 2016;92–93:617–29. Available from: http://dx.doi.org/10.1016/j.envint.2016.01.005.

104. Frampton G, Whaley P, Bennett M, Bilotta G, Dorne J-LCM, Eales J, et al. Principles and framework for assessing the risk of bias for studies included in comparative quantitative environmental systematic reviews. Environ Evid [Internet]. 2022; 11(1):1–23. Available from: https://doi.org/10.1186/s13750-022-00264-0.

105. Hoffmann S, de Vries RBM, Stephens ML, Beck NB, Dirven HAAM, Fowle JR, et al. A primer on systematic reviews in toxicology. Arch Toxicol. 2017; 91(7):2551–75. https://doi.org/10.1007/s00204-017-1980-3 PMID: 28501917

106. Coombe M, Iwasawa S, Byers KA, Prystajecky N, Hsiao W, Patrick DM, et al. A systematic review and narrative synthesis of the use of environmental samples for the surveillance of avian influenza viruses in wild waterbirds. J Wildl Dis. 2021; 57(1):1–18. https://doi.org/10.7589/JWD-D-20-00082 PMID: 33635994

107. Rodgers M, Sowden A, Petticrew M, Arai L, Roberts H, Britten N, et al. Testing methodological guidance on the conduct of narrative synthesis in systematic reviews: Effectiveness of interventions to promote smoke alarm ownership and function. Evaluation. 2009; 15(1):49–73.